

HEALTHY LONGEVITY GLOBAL COMPETITION

Accelerator Awardees

2021

Development of a Novel Alzheimer's Disease Treatment Method by a Unique Brain Proteinderived Peptide with an Advanced Transdermal Absorption Device

Catalyst Sponsor	Japan Agency for Medical Research and Development
Principal Investigator	Yasoumi Ouchi
Affiliation	Hamamatsu University School of Medicine

PROJECT DESCRIPTION

While many medical trials such as antibody therapies for amyloid to combat Alzheimer's disease (AD) are still in vain due to a difficulty in curing the disease, a new drug with a novel mechanism acting on unique targets has been expected to develop. This project entails a novel peptide drug for treating AD. The drug candidate is based on a newly discovered molecule Alcadein β which is intrinsic in the brain. Alcadein β is known to be cleaved to p3-Alc β , a brain-derived peptide that functions as a suppressor of AD progression. Experiments also show that a decrease in the p3-Alc β level in the brain relates to generation of dementia and that a peripheral administration of this peptide drug compensates its reduction, allowing to prevent from the development and progression of the disease. Removing a chance of AD onset has a great impact on the welfare in our recent longevity society. We will show substantial evidence on biochemical and pathophysiological changes in the brain before the onset of dementia and the effectiveness of our peptide drug acting on them in vitro and in vivo experimental settings using rodents and monkeys. Currently, we are performing animal experiments to verify the drug safety and a good transdermal delivery of the drug to the brain as a necessary step before first administration to the human (FIH) in a clinical trial. It is expected that the use of a newly-developed device enabling controlled transdermal absorption of the peptide drug allows the optimal drug-delivery to the brain. With a preclinical proof of concept in the efficacy of this drug in vitro and in vivo, we plan to start the clinical trial not only at an early stage of the disease but also during a preclinical period to prove its effectiveness in humans in our already-established cohorts.

Genetic Regulation of Exceptional Longevity in Rockfishes

Catalyst Sponsor	National Academy of Medicine
Principal Investigator	Stephen Treaster
Affiliation	Boston Children's Hospital and Harvard Medical School

PROJECT DESCRIPTION

Rockfishes (Sebastes genus), with nearly twenty-fold variation in longevity, are an untapped source of natural experiments in modulating, and resisting, the deleterious effects of age. The longest-lived can maintain health and function for over two hundred years, while within the group, other species survive for only eleven. Knowledge of the genetics underlying this trait would have untold therapeutic value. After a phylogenomic mapping endeavor, I have revealed genetic variation that is associated with the evolution of longevity in Rockfish. I intersected these results with human population variants, revealing significant SNPs associated with human longevity. These genes and their architecture are a powerful insight into the evolutionary toolkit for longevity, and once validated in conventional models, could be used to delay or ameliorate aging and age-related diseases.

RESPICOV-ID: Remote Assessment of Respiratory Symptoms Associated with COVID-19

Catalyst Sponsor	EIT Health of the European Union
Principal Investigator	Hans Danneels
Affiliation	Byteflies

PROJECT DESCRIPTION

During global health crises like COVID-19, healthcare systems are put under enormous pressure, often leading to patients requiring life-saving care to be turned away as resources are stretched too thin. Simple monitoring equipment for tracking fever and respiratory symptoms would already go a long way in deciding which patients to admit or discharge, provided these tools can be reliably used at home. Remote biometric monitoring technology will help prevent unnecessary patient visits and movements, reducing the chance of viral exposure. Byteflies has developed the Sensor Dot platform, a remote monitoring system that contains disposable “Smart Patches” for home use. Relevant to the problem of monitoring viral infections, Sensor Dots can monitor ECG, respiration, and motion, and we have prototypes that measure body temperature. Now, we want to fast track our solution to monitor people at increased risk of severe COVID-19 and mortality, at home.

The Next Generation of Virtual Reality Therapeutics

Catalyst Sponsor	EIT Health of the European Union
Principal Investigator	Simon Bruntse Andersen
Affiliation	Syncsense

PROJECT DESCRIPTION

We are combatting age-related inactivity. Through the development of the next generation of virtual reality therapeutics, we strive to prevent inactivity and sensory deprivation.

Currently, we are developing a digital health product that enables caregivers to deliver VR-guided physical and cognitive activity as personalised treatment which empower patients to take control of their own health. We combine R&D expertise with a human-centered approach to technology design.

Our mission is to develop digital health products that bring research, care, and technology together with the ultimate goal of helping the elderly live longer and better lives.

2022

Age-dependent trajectory of exosomal protein distribution in healthy aging and Alzheimer's disease

Catalyst Sponsor	Japan Agency for Medical Research and Development
Principal Investigator	Hoshino Ayuko
Affiliation	Tokyo Institute of Technology

PROJECT DESCRIPTION

Exosomes are small packages of proteins and genetic material that are released into the blood from various cell types and organ systems. They then flow through the blood and into other cells and organs, as a kind of cell-to-cell communication system. It has recently been discovered, however, that the messages carried within exosomes may cause numerous age-related diseases including cancer and Alzheimer's disease (AD). In this work, we aim to characterize the trajectory of how the nature of messages within exosomes change both in healthy aging and in patients that have AD. To do so, we will first use statistical characterizations of age-related changes for the healthy and AD trajectories, and try to interpret the biological significance of specific proteins. Our preliminary data already has shown that the total exosomal protein concentration increases with onset of AD. As a second approach we aim to understand what is happening at a deeper biological level. Taking inspiration from artificial intelligence (AI) approaches in modern natural language processing that use deep learning. The idea is to train a protein language model using large corpora of amino acid sequences to understand the grammar of proteins, and then fine-tune it to classify the cell types and organ systems from where exosomes are coming from. This will allow us to understand the language of the messages in exosomes, as well as the communication paths that exosomes take as they flow through the body. With this understanding, we will be able to explain the biological pathways by which exosomes act, how these pathways evolve with healthy aging, and further to make early predictions for diseases such as Alzheimer's disease.

Deep Learning to Predict Biological Age and Longevity from Chest Radiographs

Catalyst Sponsor	National Academy of Medicine
Principal Investigator	Vineet Raghu
Affiliation	Massachusetts General Hospital

PROJECT DESCRIPTION

Age-related chronic disease causes 60% of deaths in the US. Primary prevention (e.g. statin to prevent cardiovascular disease) and screening (e.g. screening for lung cancer with chest CT) interventions are based on

chronological age, but we know that chronological age is an imperfect measure of the aging process. A more accurate measure of biological age would enable healthcare providers to better personalize care and help researchers address factors underlying the aging process. The goal of our project is to develop a pragmatic measure of biological age using a convolutional neural network (CNN) and a chest x-ray image. We will evaluate whether this chest x-ray age predicts longevity and age-related disease better than chronological age. Chest x-rays are among the most common tests in medicine and leveraging these existing x-rays to more accurately assess biological age has the potential to transform care of the aging population. The CNN will be developed and tested using over 30,000 publicly available chest x-rays as well as up to 18-year follow-up for mortality in 60,000 individuals from two large multi-center clinical trials, the Prostate, Lung, Colorectal, and Ovarian (PLCO) cancer screening trial and the National Lung Screening Trial (NLST).

Designing music-based interventions for aging-related pain: Sonifying body movement using interactive mobile technology to improve physical and psychological outcomes

Catalyst Sponsor	National Academy of Medicine
Principal Investigator	Elizabeth Murnane
Affiliation	Dartmouth College

PROJECT DESCRIPTION

Music is potent medicine, positively contributing to human development, disease treatment, and overall well-being throughout the lifespan. Exploring how music-based interventions can transform how we promote healthy aging, this proposal focuses on managing pain, which increases with age and is linked with numerous aspects of functioning, mental health, and quality of life. Given the experience of pain is both physical and psycho-emotional, we propose an integrative new paradigm: leveraging music’s physiological, psychological, and neurological effects by developing interventions that combine self-expressive, music-making activities with movement-based therapies that aid pain recovery and management. We see interactive, sensor-embedded personal phones and wearables as a major opportunity to deliver and monitor the impacts of these interventions in an adaptive, personalized, and broadly scalable manner. We are particularly keen to explore musical interfaces that sonify body movement; for example, hand and finger exercises for osteoarthritis could be delivered through a virtual piano displayed on a smartphone screen, while a low-back pain patient’s reaching exercises could be sonified by mapping Fitbit gyroscope data to musical frequencies, notes, and chords. Our research will pursue the participatory design and proof-of-concept evaluation of such interactive musical interventions. Focusing on establishing feasibility, generating design guidelines, and informing technical implementation, we will examine people’s engagement with and the early efficacy of this style of intervention, in terms of short-term physical improvements (e.g., in pain intensity, impairment, proprioception) and psychological benefits (e.g., in anxiety, fear, mood, self-efficacy) as well as user experience metrics that foreshadow longer-term adoption and adherence.

Development of a Wheelchair Maintenance Alert Application for Elderly Wheelchair Users

Catalyst Sponsor	National Institutes of Health
Principal Investigator	Jon Pearlman
Affiliation	The Ohio State University

PROJECT DESCRIPTION

Elderly wheelchair users experience wheelchair breakdowns every 2-3 months in low- and middle-income countries (LMICs) and rural areas of high-income countries. One in three breakdowns leads to adverse physical, social, psychosocial and economic consequences to wheelchair users which increases the public health and personal burden. Preventative wheelchair maintenance has been found to reduce the frequency of wheelchair breakdowns by ten-fold, but compliance with maintenance recommendations is extremely low because they are generic and not reflective of how and where the wheelchair is being used. To address this issue, we are developing a low-cost, scalable maintenance application that leverages artificial intelligence tools to provide maintenance recommendations tailored to how a wheelchair is used. The availability of low-cost technology and widespread use of smartphones by the elderly and people with disabilities in LMICs has led us to develop a smartphone application called WheelTrak that measures wheelchair wear as a function of usage in community. Based on the wear factors, the application produces a Wheelchair Wear Index (WWI) that is representative of wear of critical wheelchair parts that are prone to breakdown. Once a WWI threshold is reached, maintenance is required, and the application notifies the user and/or caregiver who can conduct maintenance to avoid breakdowns and related health consequences. We will conduct a data collection study in collaboration with our wheelchair industry partner – UCP Wheels in El Salvador – and characterize the WWI for the elderly by tracking wear factors which include user's travel distance, ground shocks and surface vibrations using WheelTrak and a wheel sensor. Based on the trained WWI algorithm, a preventative maintenance schedule will be developed for older adults that can be employed through WheelTrak for maintenance reminders. Semi-structured interviews will be conducted to evaluate the usability of the application and gather barriers to maintenance. User feedback will assist us in improving WheelTrak for greater user satisfaction and compliance with maintenance and addressing any personal or logistical challenges that elderly users and their caregivers or family members may face with conducting maintenance activities in LMICs. Findings from the proposed studies in this application will assist us in planning future studies to investigate the WWI-enabled WheelTrak tool as an intervention to prevent or reduce breakdowns and health consequences with the elderly in LMICs.

Identifying Predictive Biomarkers of Effective Immunity in Aging Populations

Catalyst Sponsor	National Academy of Medicine
Principal Investigator	Wayne Koff
Affiliation	The Human Vaccines Project

PROJECT DESCRIPTION

The world is aging at an unprecedented rate, and we are not prepared. By 2050 nearly 1.6 billion people will be over age 65, creating widespread public health challenges. This aging population will dramatically increase the

burden of non-communicable diseases and enhance our vulnerability to infectious diseases. The human immune system holds the key to improving human health, and within this system lies an immense capacity for disease prevention. Technological innovations are now allowing us to reimagine and reshape the future of human health by understanding and harnessing the immune system in new ways. We have embarked on an ambitious effort to decode the human immune system, identify the biomarkers of effective immunity, and utilize this information to accelerate the development of novel therapeutics, vaccines, and diagnostics for diseases of aging populations. We use licensed vaccines to probe immunity across the age spectrum and differentiate responders from non-responders, and then utilize artificial intelligence and machine learning to develop predictive models for effective human immunity. We have recently conducted pilot trials with licensed hepatitis B and shingles vaccines in adults and elderly subjects, and performed the most comprehensive immunologic and systems biological assessment of host responses ever undertaken. Catalytic support will enable data integration and frontier supercomputing analyses to identify biomarkers of effective immunity, which we will then validate in larger-scale trials in well-studied cohorts of aging individuals. These studies may open the door for transformative new approaches to enhancing human immunity, preventing disease, and prolonging healthy lives among aging populations.

Industrialization and Preclinical Validation of a Medical Device for Microwave-Assisted Endoscopy

Catalyst Sponsor	EIT Health of the European Union
Principal Investigator	Marta Guardiola
Affiliation	MiWEndo Solutions

PROJECT DESCRIPTION

Colonoscopy is the most effective method for CRC diagnosis but still misses 22% of polyps due to visual limitations. Our value proposition is a small ring-shaped accessory attachable at the distal end of a conventional colonoscope that complements optical colonoscopy with microwave imaging that: 1) identifies automatically – with an alarm – polyps in 360° inside the colon without changing the clinical practice and 2) diagnoses the grade of dysplasia or malignancy of such identified polyps. Our target customers are endoscopists willing to improve their outcomes. MWI is a science that obtains anatomical and functional information of targets using electromagnetic waves in the regime of the microwaves based on changes in their dielectric properties. We conducted a proof-of-concept study that anticipated that the dielectric properties can univocally differentiate healthy colon mucosa, cancer, and different histological types of polyps in an ex vivo colon tissue sample study with 23 patients.

Strengthening of Osteoporotic Hips to Prevent Devastating Fractures

Catalyst Sponsor	EIT Health of the European Union
Principal Investigator	Ulrike Kettenberger
Affiliation	flowbone

PROJECT DESCRIPTION

Flowbone is a spin-off of the Swiss Federal Institute Lausanne (EPFL), founded in July 2020 after 6+ years of research and development. We aim to transform the care of elderly patients with fragile bones with the goal of preserving their mobility and independence.

Hip fractures are a huge burden: 20% of affected patients die within the first year, 50% never walk unassisted again, and the related treatment costs are very high. Anti-osteoporotic drugs, the standard of care, have a limited efficiency for the hips. Therefore, new hip-targeted, local approaches are required for hip fracture prevention, a \$2.6 billion addressable opportunity in the US, growing at 8% per year.

At flowbone, we develop the most physiological minimal-invasive treatment for local bone strengthening. Under local anesthesia and fluoroscopy, our new generation of patented biomaterial, provided in a pre-filled, ready-to-use syringe, is injected into the fragile hips. The hydrogel-based material flows smoothly into zones of low bone density, while preserving bone vascularization and biomechanics. Once in place, it triggers the body to recruit its own minerals to form a scaffold that allows fragilized bone to augment and repair itself. Pilot animal studies in rats and sheep have shown a turnover of the material into viable, new bone within only a few weeks. So far, we raised close to \$1 million non-dilutive money to finance our operations and initiate preclinical studies. We still need about \$2 million to complete the pre-clinical phase and get FDA approval for a first-in-human study in 2024.

Unraveling the Mycobiome: Fungi as a novel class of probiotics to target inflammaging

Catalyst Sponsor	National Academy of Medicine
Principal Investigator	Douglas Kiel
Affiliation	Solarea Bio

PROJECT DESCRIPTION

An aging population has led to a significant global increase in age-related diseases including cardiovascular disease, Alzheimer’s, and others. At the core of this is chronic low-grade inflammation known as inflammaging, and recent evidence describes the gut microbiome as a key regulator of the inflammaging process through direct impact on immune system development and function. Studies have demonstrated the efficacy of probiotic bacteria in treating inflammatory disorders through several biological processes (epigenetic alteration, mitochondrial dysfunction, others) known as hallmarks of aging. While the impact bacteria have on the immune system and human health is well described, fungi, a major component of the gut microbiome (mycobiome) have been largely overlooked due to multiple factors including fungi’s large, complex genomes that require deep sequencing and a hybrid assembly, lack of fungal genome databases for functional gene prediction, and underdeveloped bioinformatic tools to identify fungal metabolites important to human health. We hypothesize the mycobiome could offer a large, untapped reservoir of probiotic fungi with the ability to combat inflammaging. Given this, we propose to sequence a subset of our fungal collection with Nanopore technology and develop bioinformatic tools to complete hybrid assembly, annotation, and gene prediction to identify fungi with probiotic potential. Further, we will assess candidate strains with in vitro cell culture systems to identify fungi with anti-inflammatory properties to be tested in vivo. Here, we have the opportunity to discover safe and novel fungal agents and open an entirely new class of probiotics to specifically reduce inflammaging and related chronic illness.

WoundLAB

Catalyst Sponsor	EIT Health of the European Union
Principal Investigator	Vincent Bouchiat
Affiliation	Grapheal

PROJECT DESCRIPTION

Grapheal is developing WoundLAB as digital assistant for a wound care. It is based on an innovative electronic patch enabling continuous remote monitoring of wound healing. It involves novel bioelectronic material (graphene) as a sensing material that measures the wound conditions remotely at the wound bed without interfering with healing. Its main function consists in spotting early infections of wounds, and more particularly in the case of patients suffering of chronic wounds such as elderly and diabetics. The product is intended to be used under prescription of a medical doctor and applied under the supervision of nurses.